Medication Route Interchange - Adult - Inpatient Clinical Practice Guideline

Table of Contents

Note: Active Table of Contents -- Click to follow link

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Executive Summary

Guideline Overview

This purpose of this guideline is to identify medications clinically appropriate to automatically change the route of administration based on bioavailability, safety and efficacy data. This document provides criteria for safe and effective change in route of medication administration for inpatients (between parenteral and enteral and within the enteral route including administration via various feeding tubes).

Companion Documents

Medication Route Interchange Protocol
Dosing of Medications in Patients Receiving Continuous Enteral Feedings – Clinical Practice Guideline
Adult Enteral Nutrition Support Handbook
UW Health Electrolytes (Intravenous – Adult – Inpatient Clinical Practice Guideline
UW Health Electrolytes (Oral and Enteral) – Adult – Inpatient Clinical Practice Guidelines
UW Health Fosphenytoin and Phenytoin - Pediatric/Adult – Clinical Practice Guideline
UW Health Intravenous Administration of Formulary Medications – Adult – Inpatient Clinical Practice Guideline

Pertinent UW Health Policies & Procedures

Hospital Administrative Policy 8.17 - Administration of Medications
Hospital Administrative Policy 8.33 – High Alert Medication Administration

Patient Resources – none

Scope

Intended Users: Pharmacists, nurses, midlevel providers, physicians

CPG objective(s):

1. Identify criteria for safe and effective interchange of medication routes including intravenous, oral and feeding tube administration.
2. Identify medications clinically appropriate to change the administration route based on bioavailability, pharmacokinetic, safety and efficacy data.

Target Population:

Adult inpatients

Interventions and Practices Considered:

Providing the safest and most appropriate route of administration for medications included in this guideline.

Major Outcomes Considered:

Medication orders with the appropriate route of administration

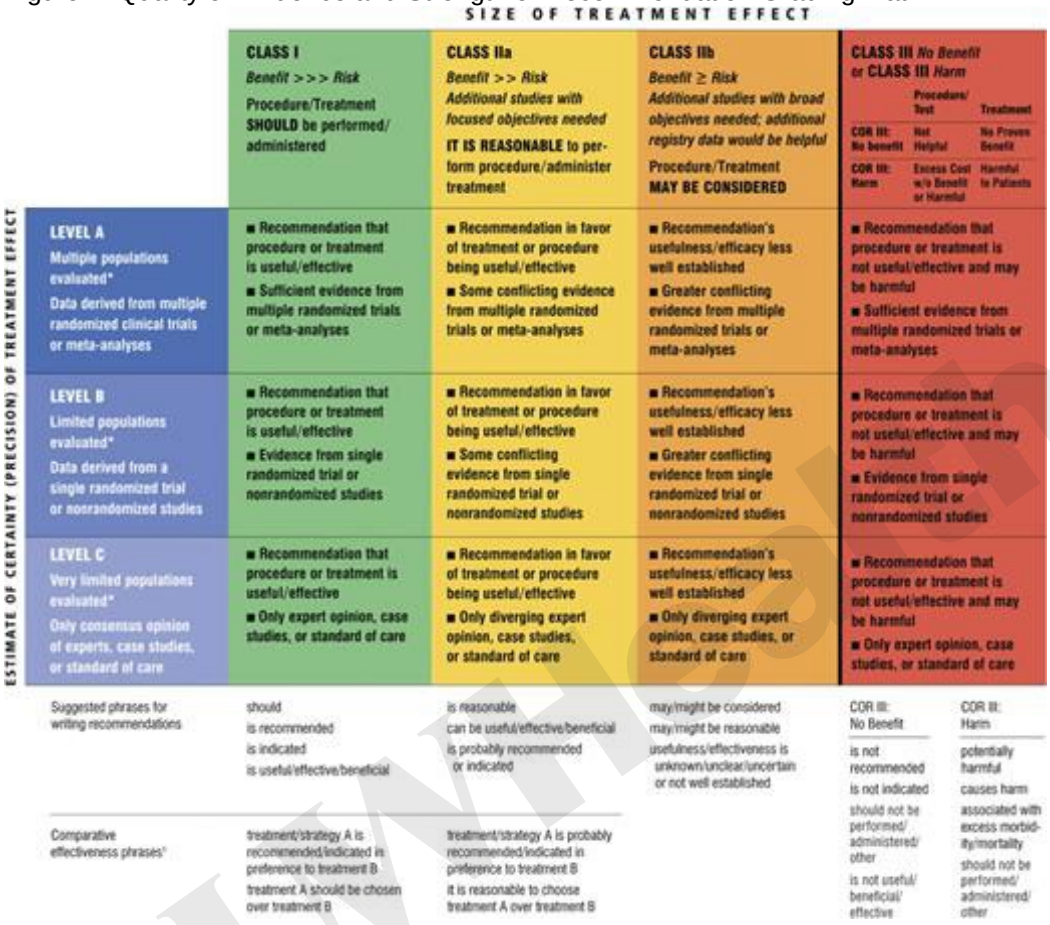
Guideline Metrics:

Compliance with the route interchange guideline and protocol.

Methodology

A modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology (Figure 1.) has been used to assess the Quality and Strength of the Evidence in this Clinical Practice Guideline.[1]

Figure 1. Quality of Evidence and Strength of Recommendation Grading Matrix



Introduction

The enteral route of medication administration is preferred over the intravenous route for improved safety, increased patient comfort, and decreased cost.[2] The intravenous route of medication administration is classified as an independent risk factor for having an adverse drug event (ADE) and is considered a high-risk activity due to the potential for error resulting from the multiple necessary complex steps.[3-5] Studies demonstrate that intravenous medication administration is associated with a 3% higher risk for ADE per each medication administered.[4] The magnitude of harm resulting from these errors has also contributed to its high-risk classification.[4,5] Furthermore, enteral administration may reduce the risk of intravenous catheter related infections, medication incompatibilities, and thrombophlebitis.[2,6] Increased costs, length of stay, and significantly higher mortality (versus other medication errors) have all been linked to intravenous administration of medications.[7,8] Intravenous administration of medications should be minimized whenever possible by encouraging conversions to oral route whenever possible.[4] Enteral medication is associated with decreased cost in comparison to intravenous medications and associated lines, sets, and infusion pumps necessary for administration. Early interchange to oral medications has been linked to shorter lengths of stay without clinical outcome compromise, independent of ADEs.[9,10]

Criteria for inclusion of medications in the guideline were high oral bioavailability and good enteral tolerance.[11] Medications were included in this guideline based upon clinical data confirming tolerability and high oral bioavailability.

Recommendations

1. **Parenteral to enteral**
   - 1.1. To initiate the parenteral to enteral interchange, which includes medications administered orally or via feeding tubes, the medication must be listed in Table 1. In addition, patients must meet all inclusion criteria and none of the exclusion criteria.
   - 1.2. Inclusion Criteria (Class 1, Level C)
     - 1.2.1. Patient must have a diet order and be tolerating either a clear liquid or more advanced diet or must be tolerating enteral tube feedings.[9]
     - 1.2.2. For antibiotics, patient's fever and white blood cell count must be down trending for the past 24 hours.[11,12]
   - 1.3. Exclusion Criteria (Class 1, Level C)
     - 1.3.1. Patient is unable to swallow, is strict NPO and without feeding tube, or refuses oral medications.[9]
     - 1.3.2. Severe vomiting or diarrhea has been documented within the past 24 hours or patient has an acute condition that affects gastrointestinal absorption (i.e., gastrointestinal obstruction or bleed, ileus, grade III or IV mucositis, gastrointestinal transit time too short for absorption, malabsorption syndromes, partial/total removal of the stomach, or short bowel syndrome.
     - 1.3.3. Patient is hemodynamically unstable (sustained heart rate >100 beats/minute, respiratory rate >24 breaths/minute, systolic blood pressure <90 mmHg or on high-doses of vasopressors in presence of shock).[13]
     - 1.3.4. Patient requires continuous tube feedings that cannot be interrupted and patient requires a medication known to bind to enteral nutrition formulas.[13]
     - 1.3.5. Patient with endocarditis, meningitis, brain abscess, orbital cellulitis, CNS infection, osteomyelitis, or endophthalmitis that should be treated with intravenous antibiotic therapy.[12]

2. **Enteral to parenteral**
   - 2.1. For a patient to be eligible for the enteral to parenteral interchange the medication must be listed in Table 1 and the patient must meet one or more of the following clinical criteria.
   - 2.2. Inclusion Criteria (Class 1, Level C)
     - 2.2.1. Patient is unable to tolerate oral medications or has failed a swallow study and does not have a feeding tube in place.[9]
     - 2.2.2. Patient has an acute condition that affects gastrointestinal absorption (i.e., gastrointestinal obstruction or bleed, severe diarrhea, ileus, severe vomiting or grade III or IV mucositis).[13]
     - 2.2.3. Patient is nutritionally compromised and parenteral administration of medication is clinically warranted to minimize the amount of time the enteral nutrition is interrupted (e.g., phenytoin, fluoroquinolones, etc.).[13]
     - 2.2.4. Patient has had an NPO order for two days or more.[9]
     - 2.2.5. Patient requires continuous gastric suctioning.[13]
   - 2.3. Exclusion criteria
     - 2.3.1. Acetaminophen, isavuconazole, posaconazole, and voriconazole cannot be converted from enteral to parenteral formulation.
     - 2.3.2. In liver, kidney and pancreas transplant patients, ganciclovir for treatment of **CMV disease or other viral infection** cannot be converted from enteral to parenteral formulation without a prescribing provider order.

3. **Enteral to enteral (oral to feeding tube and feeding tube to oral)**
   - 3.1. Medication orders with an enteral route of administration are eligible for this interchange. An initial medication order must be documented in the medical record to initiate the interchange. The pharmacist will modify the medication order based on the below inclusion criteria and evaluation of assessment criteria.

3.2. Assessment Criteria (Class 1, Level C)
- 3.2.1. Evaluation of available alternative dosage forms including an assessment of formulation appropriateness and modification of dosage and/or frequency of product if therapeutically warranted.
- 3.2.2. Assessment of drug pharmacokinetic parameters including the site of drug action, bioavailability, absorption characteristics and the effects of food on drug absorption.
- 3.2.3. Evaluation of the type of feeding tube and placement location within the gastrointestinal tract.
- 3.2.4. Assessment and modification of dosage and/or frequency if therapeutically warranted (i.e., phenytoin capsules to phenytoin suspension). A pharmacist is also permitted to modify an extended release product to an immediate release product if listed in Appendix A, Table 2 (i.e., divalproex sodium to valproic acid solution).

3.3. Oral to Feeding Tube Inclusion Criteria (Class 1, Level C)
- 3.3.1. To qualify for the oral to enteral interchange an enteral feeding tube there must be documentation of appropriate placement and approval for use
- 3.3.2. Extended Release to Immediate Release Product Inclusion Criteria (Class 1, Level C)
  - 3.3.2.1. A patient is currently ordered an extended release product and no longer able to take medications by mouth and qualifies for conversion to administration by feeding tube.
  - 3.3.2.2. Extended release product for conversion is listed in Appendix A, Table 2.

3.4. Feeding Tube to Oral Inclusion Criteria (Class 1, Level C)
- 3.4.1. To initiate a feeding tube to oral interchange the patient must have passed a swallow study as documented in the EMR.
- 3.4.2. Immediate Release to Extended Release Product Inclusion Criteria (Class 1, Level C)
  - 3.4.2.1. A patient who had previously been converted to immediate release product from extended release product who now qualifies for feeding tube to oral inclusion criteria (3.2.1).
  - 3.4.2.2. Extended release product for conversion is listed in Appendix A, Table 2.

4. **Documentation**

4.1. Medication orders meeting the above criteria for the change in the route of administration are subject to interchange as soon as the patient meets the established criteria.

4.2. Once a patient meets the criteria, the pharmacist will discontinue the current medication order and automatically convert the medication to the appropriate corresponding dosage form by placing an order in the EMR.

4.3. The pharmacist will document all protocol directed route interchanges in the electronic health record.

UW Health Implementation

Potential Benefits/Harms:

Benefits of guideline implementation include decreased length of stay, decreased cost of medication therapy, increased patient comfort, and decreased risk associated with intravenous administration of medications.

Qualifying Statements

As new data becomes available for safety and efficacy of route administration of medications recommendations may change.

Implementation Plan/Tools

1. Guideline will be housed on U-Connect in a dedicated folder for CPGs.
2. Links to this guideline will be updated and/or added in appropriate Health Link or equivalent tools.

Disclaimer

CPGs are described to assist clinicians by providing a framework for the evaluation and treatment of patients. This Clinical Practice Guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

References:

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Appendix A

Table 1. Medications Approved for Parenteral and Enteral Route Interchange

*See LexiComp "Do not crush" list for applicability of crushing tablets.

Parenteral Regimen	Parenteral Dose/Frequency	Oral Regimen	Oral Dose/Frequency	Notes
Acetaminophen*[14] *Do not convert from enteral to parenteral without provider order.	1000 mg IV	Acetaminophen	1000 mg orally	1 to 1 dosing
	650 mg IV		650 mg orally	
	325 mg IV		325 mg orally	
Azithromycin[14]	250 mg IV	Azithromycin	250 mg orally daily	1 to 1 dosing
	500 mg IV		500 mg orally daily	
Ciprofloxacin[2,11,15]	200 mg IV every 12h	Ciprofloxacin Tablet	250 mg orally twice daily	For administration via feeding tube see Lexicomp administration information Do not administer suspension via a feeding tube
	400 mg IV every 12h		500 mg orally twice daily	
	400 mg IV every 8h OR 600 mg IV every 12h		750 mg orally twice daily	
Dexamethasone[11]	2 mg IV	Dexamethasone	2 mg orally	1 to 1 dosing
	4 mg IV		4 mg orally	
	6 mg IV		6 mg orally	
	10 mg IV		10 mg orally	
Doxycycline[2]	100 mg IV	Doxycycline	100 mg orally	1 to 1 dosing
Fosphenytoin[11]	18-20 mg IV Phenytoin Equivalent (PE)/kg (loading)	Phenytoin	18-20 mg/kg in 2-3 divided doses orally (given 2 to 4 hours apart use suspension or chew tabs)	Round to nearest 100 mg and 30 mg capsule strength when converting to capsules. Round to nearest 25 mg for chew tab and 50 mg for suspension. For administration via feeding tube see Lexicomp administration information, Lexicomp food interactions, and Fosphenytoin and Phenytoin Guideline
	4-6 mg IV PE/kg/day		Chew tabs/suspension: 4-6 mg/kg/day in 2 divided doses Capsules: 1-2 divided doses orally (once daily if dose <400 mg)	
Fluconazole[11]	100 mg IV	Fluconazole	100 mg orally	1 to 1 dosing
	200 mg IV		200 mg orally	
	400 mg IV		400 mg orally	
Ganciclovir (IV)[14] **FOR CMV PROPHYLAXIS** For kidney and pancreas transplant patients, may convert to oral when tolerating oral[#]	**Based on Creatinine Clearance**	Valganciclovir (PO)	**Based on Creatinine Clearance**	Valganciclovir is the oral prodrug of ganciclovir Note: CrCl cut-offs vary from IV to PO formulation Dose-reduced valganciclovir is a risk factor
	> 70 mL/min 5 mg/kg every 24 hr		**> 60 mL/min** 900 mg once daily	
	50-69 mL/min 2.5 mg/kg every 24 hr		**40-59 mL/min** 450 mg once daily	
	25-49 mL/min 1.25 mg/kg every 24 hr		**25-39 mL/min** 450 mg once every OTHER day	

Parenteral Regimen	Parenteral Dose/Frequency	Oral Regimen	Oral Dose/Frequency	Notes
For liver transplant patients, may convert to oral after transfer from ICU to General Care[#]	**10-24 mL/min** 0.625 mg/kg every 24 hr		**10-24 mL/min** 450 mg twice weekly	for ganciclovir-resistant CMV. Consider alternative prophylaxis approaches or select the higher dose for borderline or improving creatinine clearance. #For ganciclovir, if BMI > 30 kg/m^2, use adjusted body weight. If BMI < 30 kg/m^2, use actual body weight
	< 10 mL/min (HD) 0.625 mg/kg three times weekly after hemodialysis		**<10 mL/min or HD** 100mg three times weekly after hemodialysis *If oral solution is not covered by insurance, 450 mg twice weekly administered post-HD on M/F or Tu/Sa is reasonable	
Ganciclovir (IV)[14] FOR CMV TREATMENT	**If ganciclovir is used for treatment of CMV disease (or other viral infection), the route interchange may NOT be used. If ganciclovir is used for CMV prophylaxis, please see row above for conversion to PO valganciclovir.**			
Isavuconazole*[14] *Do not convert from enteral to parenteral without provider order.	372 mg (isavuconazole 200 mg) every 8 h	Isavuconazole	372 mg (isavuconazole 200 mg) every 8 h	1 to 1 dosing
Lacosamide[14]	50 mg IV	Lacosamide	50 mg orally	1 to 1 dosing
	100 mg IV		100 mg orally	
	150 mg IV		150 mg orally	
	200 mg IV		200 mg orally	
Levetiracetam[11]	500-1500 mg IV	Levetiracetam	500-1500 mg orally	1 to 1 dosing
Levofloxacin[14]	500-750 mg IV once daily	Levofloxacin	500-750 mg PO once daily	For administration via feeding tube see Lexicomp administration information, Lexicomp food interactions
Levothyroxine[11,16,17]	15 mcg/day IV	Levothyroxine	25 mcg orally daily	Parenteral dose should be approx. 80% of oral dose[16,17] For administration via feeding tube see Lexicomp administration information
	35 mcg/day IV		50 mcg orally daily	
	50 mcg/day IV		75 mcg orally daily	
	75 mcg/day IV		100 mcg orally daily	
	85 mcg/day IV		125 mcg orally daily	
	100 mcg/day IV		150 mcg orally daily	
	125 mcg/day IV		175 mcg orally daily	
	150 mcg/day IV		200 mcg orally daily	
Linezolid[11]	600 mg IV	Linezolid	600 mg orally	1 to 1 dosing
Metoclopramide[14]	10 mg IV	Metoclopramide	10 mg orally	1 to 1 dosing
Metronidazole[14]	500 mg IV	Metronidazole	500 mg orally	1 to 1 dosing

Parenteral Regimen	Parenteral Dose/Frequency	Oral Regimen	Oral Dose/Frequency	Notes
Methylprednisolone[14]	4 mg IV	Prednisone	5 mg orally	
Moxifloxacin[2]	400 mg IV	Moxifloxacin	400 mg orally	1 to 1 dosing For administration via feeding tube see Lexicomp administration information
Mycophenolate mofetil (CellCept)[14,18] **Kidney, liver, pancreas transplant patients ONLY**	250 mg IV every 12 h	Mycophenolate **mofetil** generic	250 mg twice daily	*When converting 1000 mg from IV to enteral, base enteral dose on home regimen or UW Health transplant regimens.
	500 mg IV every 12h		500 mg twice daily	
	750 mg IV every 12h		750 mg twice daily	
	1000 mg IV every 12h		1000 mg 2-3 times daily*	
Mycophenolate mofetil (CellCept)[14,18] **Kidney, liver, pancreas transplant patients ONLY**	250 mg IV every 12 h	Mycophenolate **sodium** (Myfortic)	180 mg twice daily	*When converting 1000 mg from IV to enteral, base enteral dose on home regimen or UW Health transplant regimens.
	500 mg IV every 12h		360 mg twice daily	
	750 mg IV every 12h		540 mg twice daily	
	1000 mg IV every 12h		720 mg 2-3 times daily*	
Ondansetron[14]	4mg IV	Ondansetron orally disintegrating tablet (ODT)	4mg ODT	1 to 1 dosing
Pantoprazole[11,19]	40 mg IV	Pantoprazole	40 mg orally	1 to 1 dosing
Phenobarbital	1-3 mg/kg/day IV (2 divided doses)	Phenobarbital	1-3 mg/kg/day orally (1-2 divided doses)	Only maintenance dosage qualifies for interchange
Phenytoin[2,11]	18-20 mg IV PE/kg (loading)	Phenytoin	18-20 mg/kg in 2-3 divided doses orally	Round to nearest 100 mg and 30 mg capsule strength when converting to capsules. Round to nearest 25 mg for chew tab and 50 mg for suspension. For administration via feeding tube see Lexicomp administration information, Lexicomp food interactions, and Fosphenytoin and Phenytoin Guideline
	4 to 6 mg/kg IV/day		Chew tabs/suspension: 4-6 mg/kg/day in divided doses Capsules: 1-2 divided doses orally (once daily if dose <400 mg)	
Posaconazole*[14] *Do not convert from enteral to parenteral without provider order.	300 mg IV daily	Posaconazole	300 mg PO daily delayed-release tablet	1 to 1 dosing

Parenteral Regimen	Parenteral Dose/Frequency	Oral Regimen	Oral Dose/Frequency	Notes
Potassium Chloride	10 mEq - 40 mEq IV	Potassium Chloride	10 mEq - 40 mEq orally	1 to 1 dosing Doses ≥ 40 mEq should be given in increments of 20mEq at 2-hour intervals See: Guideline for Use of Oral and Enteral Electrolytes in Adults
Rifampin	600 mg IV	Rifampin	600 mg orally	1 to 1 dosing
Sulfamethoxazole-trimethoprim	320/1600 mg 160/800 mg	Sulfamethoxazole -trimethoprim	320/1600 mg 160/800 mg	1 to 1 dosing
Valproic Acid	10-15mg/kg/day IV (divided every 6 hr)	Divalproex Valproic Acid solution	Immediate release 3-4x orally daily; delayed release 2-3 x orally daily; 10-15mg/kg/day	Round dose to nearest tablet strength
Voriconazole*[2] *Do not convert from enteral to parenteral without provider order.	4 mg/kg IV every 12h or 200-400 mg IV every 12	Voriconazole	4 mg/kg PO every 12h (susp) or 200-400 PO every 12h	Round to the nearest tablet strength using tablets For administration via feeding tube see Lexicomp administration information

Table 2. Oral to Enteral Tube Route Interchanges

Oral Formulation	Dose/Frequency	Enteral Tube Formulation	Dose/Frequency	Notes
Bupropion ER	150 to 400 mg/day	Bupropion	50 to100 mg 3-4 times daily	1 to 1 daily dose conversion with increased frequency
Carbamazepine ER	200 mg/day	Carbamazepine	200 mg/day in divided doses	Same total daily dosage divided two to four times daily
	400 mg/day		400 mg/day in divided doses	
	600 mg/day		600 mg/day in divided doses	
	800 mg/day		800 mg/day in divided doses	
Carbidopa/levodopa 25/100 mg ER	25/100 to 200/800 mg twice daily	Carbidopa/levodopa 25/100 mg	40/160 to 320/1280 mg/day in divided doses	Convert dose based on levodopa equivalents. Give 80% of the total daily levodopa ER dose as immediate release levodopa. Divide calculated total daily dose into three or four times daily dosing. Round doses to the nearest 50 mg.
Diltiazem HCL ER 24hr	120 mg/day	Diltiazem	30 mg four times daily	
	180 mg/day		45 mg four times daily	
	240 mg/day		60 mg four times daily	
	300 mg/day		75 mg four times daily	
Divalproex Sodium ER	500 mg/day	Valproic Acid Solution	500 mg/day in divided doses	Same total daily dosage divided three times daily
	1000 mg/day		1000 mg/day in divided doses	
Isosorbide Mononitrate ER	30 mg/day	Isosorbide Mononitrate	10 mg TID	Patient must have at least 12 hour nitrate-free period
Metoprolol Succinate ER	25 mg/day	Metoprolol Tartrate	12.5 mg twice daily	Same total daily dosage
	50 mg/day		25 mg twice daily	
	100 mg/day		50 mg twice daily	
	200 mg/day		100 mg twice daily	
Morphine Sulfate ER	90 mg/day	Morphine Sulfate	15 mg every 4 hr	Only listed doses may be converted; all other doses require provider order
	180 mg/day		30 mg every 4 hr	
	270 mg/day		45 mg every 4 hr	
Oxycodone ER	30 mg/day	Oxycodone	5 mg every 4 hr	Only listed doses may be converted; all other doses require provider order
	60 mg/day		10 mg every 4 hr	
	90 mg/day		15 mg every 4 hr	
Potassium Chloride ER	10 mEq	Potassium Chloride Solution	10 mEq	1 to 1 conversion at same frequency
	20 mEq		20 mEq	
Probiotic capsule	1 cap daily	Probiotic suspension	1.2 mL daily	
	2 caps daily		2.4 mL daily	
Propranolol SR	60 mg/day	Propranolol	20 mg three times daily	
	80 mg/day		20 mg four times daily	
	120 mg/day		30-40 mg 3-4 times daily	
	160 mg/day		40 mg four times daily	
Venlafaxine ER	75 to 225 mg/day	Venlafaxine	37.5 to 75 mg 2-3 times daily	1 to 1 dose conversion

Oral Formulation	Dose/Frequency	Enteral Tube Formulation	Dose/Frequency	Notes
Verapamil HCL ER	120 mg/day	Verapamil	40 mg three times daily	
	180 mg/day		60 mg three times daily	
	240 mg/day		80 mg three times daily	